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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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Kim Vilbour Andersen

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EXAMINER

LIU, SAMUEL W

ART UNIT

PAPER NUMBER

1656

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PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

<b>Office Action Summary</b>	<b>Application No.</b> 10/549,506	<b>Applicant(s)</b> ANDERSEN ET AL.	
	<b>Examiner</b> SAMUEL W. LIU	<b>Art Unit</b> 1656	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 15 May 2009.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 1,3-17,54-59 and 65-68 is/are pending in the application.
- 4a) Of the above claim(s) 55-58 and 65-68 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1,3-7,14-17,54 and 59 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 16 September 2005 is/are: a) ☒ accepted or b) ☒ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |   |   |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)   | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftperson's Patent Drawing Review (PTO-948)   | 5) <input type="checkbox"/> Notice of Informal Patent Application                       |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)<br>Paper No(s)/Mail Date <u>11/16/06, 7/20/06, 6/28/07, 2/6/07 &amp; 7/30/07</u> . | 6) <input checked="" type="checkbox"/> Other: <u>attached "Notice to comply"</u> .      |



**DETAILED ACTION**

**Status of claims**

Claims 1, 3-17, 54-59 and 65-68 are pending.

The preliminary amendment filed 9/16/2005 which amends claims 1, 3, 6, 13, 14, 17, 54, 55, 57, 59, and 65, and cancels claims 2, 18-53 and 60-64 has been entered.

***Claim benefit***

Applicant's claim for the benefit of a prior-filed application 60456547 filed 3/20/03 and 60479708 filed 6/19/03 under 35 U.S.C. 119(e) is acknowledged. Both applications have support for the claimed invention (see below).

***IDS***

The references listed in the IDS documents filed 11/16/06, 7/20/06, 6/28/07, 2/6/07 and 7/30/07 have been considered by Examiner. In the 11/16/06 IDS, reference 40 has been edited to remove reference to the hypertext.

***Election/Restrictions***

Applicants' election filed 5/15/09 of Group I, claims 1, 3-17, 54 and 59 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)). Claims 55-58 and 65-68 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention. Claims 1, 3-17, 54 and 59 are under examination.

***Objection to specification***

The disclosure is objected to because of the following informalities:

(1) At page 5, lines 20 and 21, “• rhFVIIa” “□ G237GAA” should be deleted because it belongs to the drawing of Figure 1 which already indicates this (see Figure 1).

(2) At page 23, line 10, “PEG” should be spelled out in full for the first instance of use. See also, page 24, line 15, “VS-PEG”.

(3) At page 31, line 32, trade name “NovoSeven®”. It should be capitalized wherever it appears and be accompanied by the generic terminology. Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks. See also page 37, line 8.

(4) At page 44, the term "Table 1" should be moved to the top of the table thereof.

***Objection to claims***

Claims 1, 3-17, 54 and 59 are objected to because, in claim 1, (i) “position” should be changed to residue for consistency (see claim 10 and the specification p. 1, line 25 where use the term “residue” instead of “position”); see also claims 3, 16 and 14; (ii) “FVII” and “FVIIa” should be spelled out in full upon the first recitation in the claims; and (iii) after “including at least one amino acid modification .... 196, 237 and 341” should insert “of SEQ ID NO:2” in order to explicitly indicate that the residues “196, 237 and 341” refer to SEQ ID NO:2.

Comment [A1]:

In claim 11, after “consisting” and before “Ala”, should insert "of".

***Sequence Compliance***

This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 C.F.R. 1.821(a)(1) and (a)(2).

However, this application fails to **fully** comply with the requirements of 37 C.F.R. § 1.821 through 1.825; Applicants' attention is directed to the final rulemaking notice published at 55 FR 18230 (May 1, 1990), and 1114 OG 29 (May 15, 1990).

At page 25, lines 26 and 27, one amino acid sequence "GAAA" is disclosed without SEQ ID NO identification. See also "Notice to Comply". See the attached "Notice to comply".

***Claim Rejections - 35 USC § 112, second paragraph***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter that the applicant regards as his invention.

Claims 1, 3-17, 54 and 59 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 does not make it clear whether or not the modification at residue 196, or/and 237 or/and 341 is in reference to "hFVIIa" (SEQ ID NO:2) or "hFVII" (instant claims do not set forth SEQ ID NO: \_ for "hFVII"); in the absence of said SEQ ID NO: \_, the modification at said residue(s) cannot be determined. Claims 3-17, 54 and 59 which depend from claim 1 are also rejected.

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\* Note that the above-mentioned “hFVII” is an zymogen of its activated form “hFVIIa” which is resulted from a proteolytic cleavage of said zymogen (p.1, lines 17-19, the specification), and that amino acid sequence of “hFVII” (see Fig. 2, O’Hara et al. (1987) *Proc. Natl. Acad. Sci. USA*, 84, 5158-5162, and p.1, lines 30-32, the specification) differs from instant SEQ ID NO:2.

Similarly, claim 3 recites “...position 196 compared to hFVII or hFVIIa (SEQ ID NO:2)”; the recitation is indefinite because without setting forth SEQ ID NO: for “hFVII”, residue 196 cannot be determined. Similarly, see also, claims 6 and 14.

In claim 4, it is unclear if the “said modification” is referring to the 1-15 modifications or the at least one modifications in positions 196, 237, and 341?

Claim 10 recites “insertion is ... G237**GXX**, G237**GXXX**, G237**GXXXX**”; it is unclear whether or not the insertion includes residue “Gly”, i.e., “G237” per se or only refers to “**GXX**”, “**GXXX**” or “**GXXXX**”. Similarly, see claim 13, “G237GAA”.

Claim 17 recitation “comprises 1-10 further amino acid modification” is unclear whether or not “further” is based on the range “1-15 amino acid modification” set forth in claim 1 from which claim 17 depends, or/and a particular amino acid modification such as one modification at 196, for example.

**Comment [A2]:** Is this word “range”?  
Yes, “range”

### ***Claim Rejections - 35 USC §102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office Action:

A person shall be entitled to a patent unless -

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

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(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

[1] Claims 1, 14, 15, 17 and 54 are rejected under 35 U.S.C. 102(b) as being anticipated by Hu et al. (*Proc. Natl. Acad. Sci. USA*, (2001) 98, 12180-12185).

Hu et al. teach a purified polypeptide ("mfVII/hFc") comprising variant FVII (see p. 12181, right col., 4<sup>th</sup> paragraph, line 8) which contains a substitution at residue 341 (see "SEQ alignment attachment I, and p.12184, right col., line 5), which anticipates claims 1, 14 and 15.

In the "mfVII/hFc" polypeptide, at least one modification, in addition to said "substitution", has been modified by conjugation to a "Fc" polypeptide (see p.12180, right col., lines 11-13); wherein said "conjugation" is a type of chemical modification *via* covalently attaching "Fc" to an amino acid side chain of "FVII" polypeptide. This teaches claim 17.

Because the "variant FVII" discussed-above has sequence identity to instant SEQ ID NO:2 which is an activated form (i.e., "FVIIa") of FVII zymogen (see p.1, line 18, instant specification) except the "substitution" at residue 341, polypeptide, claim 54 is anticipated.

[2] Claims 1, 3, 14-17, 54 and 59 are rejected under 35 U.S.C. 102(b) as being anticipated by Nicolaisen et al. (WO 0238162 A1).

In patent claims 1 and 18, Nicolaisen et al. teach a modified FVIIa comprising substitution at lysine 341 and substitutions at other residues such as lysine 316, wherein "FVIIa" consists of amino acid sequence (see Fig. 1) having sequence identity with instant SEQ ID NO:2. This teaches claims 1, 3, 4, 14, 15, 17 and 54.



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The lysine 341 is substituted by Gln (i.e., K341Q), which anticipates claim 16.

Nicolaisen et al. teach a FVIIa preparation (see page 4, lines 30-35) which is equivalent to instant composition of claim 59.

[3] Claims 1, 3-7, 14, 15, 17, 54 and 59 are rejected under 35 U.S.C. 102(b) as being anticipated by Andersen et al. (WO 0158935 A2).

In patent claims 1, 34-36, 39, 41, 42 and 48-50, Andersen et al. teach a modified FVIIa (variant) polypeptide having SEQ ID NO:1 which is identical to instant SEQ ID NO:2. The variant comprises one or more substitutions including "G196N" (claim 26 and p.29, line 30), "K341N" or "K341 S/T" (claims 49-51), and "G237N" (claim 44); wherein "FVIIa" is an active form of "FVII" zymogen. This anticipates claims 1, 3-7, 14, 15, 17 and 54.

In patent claim 64, Andersen et al. teach a pharmaceutical composition comprising said modified FVIIa, which anticipates claim 59.

[4] Claims 1, 3, 14, 15, 17, 54 and 59 are rejected under 35 U.S.C. 102(a) as being anticipated by Ruf et al. (WO 0238162 A1).

In patent claims 1 and 18, Ruf et al. teach a modified FVIIa (variant) comprising a substitution of amino acid 341 (claim 18); wherein the variant is based on the amino acid sequence disclosed in US Pat. No. 6132730 ("incorporated herein by reference", see p.15, lines 1 and 2); this patent discloses that the Factor VIIa (active form of FVII) has the amino acid sequence from residues 61 to 212 of SEQ ID NO: 14 (see patent claim 5 and columns 139-142,

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6132730) wherein said amino acid sequence has sequence identity with instant SEQ ID NO:2.

Thus, Ruf et al. teach claims 1, 3, 4, 14, 15, 17 and 54.

In patent claim 9, Ruf et al. teach a pharmaceutical composition comprising the FVIIa variant, which anticipates claim 59.

***Conclusion***

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Samuel Wei Liu whose telephone number is 571-272-0949. The examiner can normally be reached from 9:00 a.m. to 5:30 p.m. on weekdays. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor Andrew Wang can be reached on 571-272-0811. The fax phone number for the organization where this application or proceeding is assigned is 703 308-4242 or 703 872-9306 (official) or 703 872-9307 (after final). Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703 305-4700.

/Samuel Wei Liu/

Patent Examiner, Art Unit 1656

/ANAND U DESAI/

Primary Examiner, Art Unit 1656

July 19, 2009